Bmps and id2a act upstream of Twist1 to restrict ectomesenchyme potential of the cranial neural crest.

Journal: PLoS Genet

Publication Year: 2012

Authors: Ankita Das, J Gage Crump

PubMed link: 22589745

Funding Grants: Skeletogenic Neural Crest Cells in Embryonic Development and Adult Regeneration of the Jaw

Public Summary:
A fascinating question of vertebrate development is how a single cell population—the cranial neural crest—creates such different types of structures as the peripheral nervous system and head skeleton. To date, the molecular signals that instruct neural crest cells to develop into head skeleton at the expense of nervous system have remained elusive. One reason why such signals have been difficult to identify is that they may be required at multiple stages of development—such as in the emergence of neural crest cells themselves. In order to overcome this challenge, we developed a transgenic system in zebrafish that allows us to alter signaling precisely at the stage when neural crest cell fates are determined. In so doing, we have found that the early movement of neural crest cells allows them to escape the influence of suppressive signals at their birthplace, which, in turn, sets in motion a cascade that turns off nervous system genes and turns on head skeleton genes. Together, our studies show how the timing of neural crest cell movement plays a major role in biasing early neural crest cells to form the head skeleton.

Scientific Abstract:
Cranial neural crest cells (CNCCs) have the remarkable capacity to generate both the non-ectomesenchyme derivatives of the peripheral nervous system and the ectomesenchyme precursors of the vertebrate head skeleton, yet how these divergent lineages are specified is not well understood. Whereas studies in mouse have indicated that the Twist1 transcription factor is important for ectomesenchyme development, its role and regulation during CNCC lineage decisions have remained unclear. Here we show that two Twist1 genes play an essential role in promoting ectomesenchyme at the expense of non-ectomesenchyme gene expression in zebrafish. Twist1 does so by promoting Fgf signaling, as well as potentially directly activating fli1a expression through a conserved ectomesenchyme-specific enhancer. We also show that Id2a restricts Twist1 activity to the ectomesenchyme lineage, with Bmp activity preferentially inducing id2a expression in non-ectomesenchyme precursors. We therefore propose that the ventral migration of CNCCs away from a source of Bmps in the dorsal ectoderm promotes ectomesenchyme development by relieving Id2a-dependent repression of Twist1 function. Together our model shows how the integration of Bmp inhibition at its origin and Fgf activation along its migratory route would confer temporal and spatial specificity to the generation of ectomesenchyme from the neural crest.